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Antibiotic prophylaxis in trauma: Global Alliance for Infection in Surgery, Surgical Infection Society Europe, World Surgical Infection Society, American Association for the Surgery of Trauma, and World Society of Emergency Surgery guidelines

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ABSTRACT: Trauma is a complex disease, and the use of antibiotic prophylaxis (AP) in trauma patients is common practice. However, considering the increasing rates of antibiotic resistance, AP use should be questioned and limited only to specific cases. Antibiotic stewardship is of paramount importance in fighting resistance spread. Definitive rules or precise indications about AP in trauma remain unclear. The present article describes the indications of AP in traumatic lesions to the head, brain, torso, maxillofacial, extremities, skin, and soft tissues endorsed by the Global Alliance for Infection in Surgery, Surgical Infection Society Europe, World Surgical Infection Society, American Association for the Surgery of Trauma, and World Society of Emergency Surgery. (*J Trauma Acute Care Surg.* 2024;96: 674–682. Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.)

KEY WORDS: Antibiotic; prophylaxis; therapy; trauma; guidelines.

Antibiotic prophylaxis (AP) in surgery is critical to prevent surgical site infections (SSIs). It is defined as the prevention of infectious complications by administering an effective antimicrobial agent before exposure to contamination during surgery.[1] As suggested by Bratzler et al.,[2] AP may also be defined as "the rational, safe, and effective use of antimicrobial agents for the prevention of (initial) SSIs."

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The World Health Organization provides strong recommendations on the administration of AP before surgical incision when indicated, depending on the type of operation and its timing and duration.[3] However, AP is often used inappropriately around the globe. Antibiotic misuse reduces patient safety and increases the rate of antimicrobial resistance. Physicians worldwide generally apply wrong criteria when prescribing AP because of errors associated with the following factors: drug, dosage, duration, timing, and/or means of administration. In polytrauma patients, the presence of multiple associated injuries may lead to multiple potential risks of infections. For this reason, antibiotics used for treatment or prophylaxis are commonly applied worldwide without a clear and defined rationale following recommended guidelines. Clinical research reflects this heterogeneous practice associated with the difficulty of standardizing definitions and approaches.[4]

The very liberal use of antibiotics and often their misuse trigger several severe problems.[5] Increased antibiotic resistance, the issues linked to infection by *Clostridioides* spp., and the urgent need to rationalize resources create a need to standardize and control AP prescription.[6] Ideally, AP in trauma should be targeted specifically for each patient, accounting for their individual characteristics. In addition, it should decrease the risk of infection due to single or multiple injuries, reduce the selection of multiresistant species, and have no adverse effects.[7] Liberal and premature administration of antimicrobials should be avoided.[8] Infections must be treated only when present, and their prevention must occur based on specific rules and precise circumstances. The fear of infections must not drive AP prescription. Specific evidence-based indications and antimicrobial stewardship programs must be implemented locally, nationally, and internationally.[9]

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The present article reports on the recommendations proposed and endorsed by the Global Alliance for Infection in Surgery, Surgical Infection Society Europe, World Surgical Infection Society, American Association for the Surgery of Trauma, and the World Society of Emergency Surgery regarding AP in head, brain, torso, maxillofacial, extremities, skin, and soft tissue injuries. We aimed to provide the indications of AP in managing trauma patients.

Notes on the Use of the Guidelines

The guidelines are evidence based, with the grade of recommendation based on the evidence. The guidelines present the methods for optimal management of AP in trauma patients. The practice guidelines promulgated in this work do not represent a standard of practice. They are suggested plans of care based on the best available evidence and the consensus of experts, but they do not exclude other approaches as being within the standard of practice. For example, they should not be used to compel adherence to a given medical management method, which should be finally determined after considering the conditions at the relevant medical institution (staff levels, experience, equipment, etc.) and the characteristics of the individual patient. However, responsibility for treatment results rests with those directly engaged therein and not with the consensus group.

PATIENTS AND METHODS

A computerized search was done by a bibliographer in different databases (MEDLINE, Scopus, EMBASE), and citations published between January 2000 to May 2023 were included when satisfying the primary search strategy: "antibiotic prophylaxis," "trauma," "antibiotic," "heat trauma," "brain trauma," "burns," "skin," "maxillofacial," "thoracic trauma," "abdominal trauma," "facial trauma," "bites," and "guidelines" combined with AND/OR. No search restrictions were imposed. Expert opinion reviews, narrative reviews, case reports, and case series based on less than 30 patients were not considered relevant. The dates were selected to allow comprehensive published abstracts of clinical trials, consensus conferences, comparative studies, congresses, guidelines, government publications, multicenter studies, systematic reviews, meta-analyses, large case series, original articles, and randomized controlled trials (RCTs). Narrative review articles were only used to determine if other cited studies should be included.

The level of evidence was graded as high, moderate, low, and very low. The grade of recommendation, defined as strong, moderate, and weak, was established, considering the Oxford model.[10]

A group of experts from the involved Societies (Global Alliance for Infection in Surgery, Surgical Infection Society Europe, World Surgical Infection Society, American Association for the Surgery of Trauma, and World Society of Emergency Surgery) led by a central coordinator was contacted to express their evidence-based position on the topic. Through the Delphi process, different issues were discussed in several rounds. The central coordinator assembled the different answers derived from each round. Each version was then revised and improved. After three rounds, the process led to 100% agreement on all statements. The final version upon which the agreement was reached resulted in the present article. Statements are summarized in Table 1.

DEFINITIONS

Antibiotic prophylaxis, defined as the use of antibiotics to prevent infections at the site of injury and/or surgical site, must be administered close to the time of procedure initiation or time of injury and according to its pharmacodynamics and pharmacokinetics.

Prolonged AP is defined as AP extending beyond the first 24 hours after an invasive procedure or injury.

Antibiotic therapy is defined as the use of antibiotics aiming to provide adequate drug activity (bacteriostatic or bactericidal) at the site of infection against defined/undefined bacteria. It should exceed the amount needed to inhibit the growth of the microorganism involved and/or kill it.

Head and Brain Trauma

- Antibiotic prophylaxis in blunt head and brain trauma is not indicated in patients treated nonoperatively (moderate recommendation, intermediate-quality evidence).
- Prolonged AP (24 hours) in penetrating head and brain trauma is indicated (moderate recommendation, intermediate-quality evidence).

Blunt head and brain traumas are the most frequent mechanisms of injury, although penetrating injury is prevalent in some regions of the world. The literature on antibiotic therapy in those injuries is generally scarce, and the quality of evidence is low. However, based on the published studies, some indications are clear. No significant differences in infection rates exist between patients who received AP and those who did not.[11–21] No differences were observed between basilar or skull close and open fractures.[22] Data showed heterogeneity in terms of inclusion criteria, duration of antibiotic therapy, and dosages.[13,14] It must be emphasized that differences exist regarding the definition of AP and the timing of administration among different studies published during the last decades. These differences may impair the possibility of obtaining definitive data. Prolonged AP was administered with different drugs (5-day ceftriaxone, 3-day ceftriaxone or ampicillin-sulbactam, and 8-day average course of penicillin, respectively), but the existence of antibiotic-resistant bacteria was not investigated.[23–25]

Maxillofacial Trauma

- Antibiotic prophylaxis in blunt maxillofacial trauma is indicated in patients undergoing open reduction of the fracture (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis in penetrating maxillofacial trauma is indicated (moderate recommendation, intermediate-quality evidence).
- Prolonged AP (24 hours) may be considered in cases of open reduction of contaminated wounds (moderate recommendation, low-quality evidence)

Infection is the most common complication in open mandibular fractures (10–15%).[26] A possible source of contamination is the colonization of the oral cavity. Fractures involving this site could be considered contaminated.[27] No consensus in AP administration for operative and nonoperative facial fractures

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TABLE 1. Summary Statements

	Summary Statements
Head and brain trauma	– Antibiotic prophylaxis in blunt head and brain trauma is not indicated in patients treated nonoperatively (moderate recommendation, intermediate-quality evidence). – Prolonged AP (24 hours) in penetrating head and brain trauma is indicated (moderate recommendation, intermediate-quality evidence).
Maxillofacial trauma	– Antibiotic prophylaxis in blunt maxillofacial trauma is indicated in patients undergoing open reduction of the fracture (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis in penetrating maxillofacial trauma is indicated (moderate recommendation, intermediate-quality evidence). – Prolonged AP (24 h) may be considered in cases of open reduction of contaminated wounds (moderate recommendation, low-quality evidence).
Thoracic trauma	– Antibiotic prophylaxis in healthy patients sustaining blunt thoracic trauma is not indicated (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is not indicated in blunt thoracic trauma patients undergoing chest tube placement (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is indicated in penetrating thoracic trauma patients undergoing chest tube placement (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is indicated in all cases of delayed drainage of retained hemothorax (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is indicated in blunt and penetrating thoracic trauma cases undergoing surgical exploration (thoracotomy/thoracoscopy) (moderate recommendation, intermediate-quality evidence).
Abdominal trauma	– Antibiotic prophylaxis is not indicated in blunt abdominal trauma treated nonoperatively (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is indicated in penetrating abdominal trauma, especially in patients undergoing surgical exploration (laparotomy/laparoscopy) (moderate recommendation, intermediate-quality evidence). – Prolonged AP (24 h) and/or antibiotic therapy should be considered in patients with hollow viscus injury (moderate recommendation, intermediate-quality evidence).
Open fractures	– Antibiotic prophylaxis effectively reduces wound infections in open fractures, and it should be administered as soon as possible (moderate recommendation, intermediate-quality evidence). – Long-term antibiotic treatment (7–10 d) is ineffective in reducing open fracture wound infection rate (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis longer than 24 h is not indicated in gunshot-related fractures (moderate recommendation, intermediate-quality evidence).
Burns	– Routine AP in burns patients is not indicated (moderate recommendation, intermediate-quality evidence). – Routine source control with extensive irrigation for the removal of contaminated material is part of infection prevention in burn patients (moderate recommendation, intermediate-quality evidence). – No differences exist between systemic and topical AP in preventing infections in burn patients (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis in severe burn patients is indicated in those undergoing endotracheal intubation and mechanical ventilation; it should be ideally administered before the intubation and according to the pharmacokinetics of the chosen antibiotic when possible (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis in severe burn patients may be indicated to prevent split-thickness skin graft infection (moderate recommendation, intermediate-quality evidence). – There is no indication for routine AP following the debridement of devitalized tissues (moderate recommendation, intermediate-quality evidence).
Skin wounds and bites	– Routine AP in skin and soft-tissue injuries is not strictly indicated and should be considered case by case (moderate recommendation, intermediate-quality evidence). – Routine AP in mammalian bites is not strictly indicated and should be considered case by case (moderate recommendation, intermediate-quality evidence). – Accurate prevention of viral infectious disease in animal bites must be performed (i.e., rabies virus) (moderate recommendation, intermediate-quality evidence). – Attention to tetanus immunization must be given (moderate recommendation, intermediate-quality evidence). – Accurate source control should be accomplished by cleaning, irrigating, and disinfecting wounds in all skin and soft tissue injuries, including all mammalian bites (moderate recommendation, intermediate-quality evidence).

exists.[28] In general, no differences exist related to the location of the fracture (condylar, maxillary, zygoma) or among different classes of antibiotics in terms of infectious complications due to AP use. Antibiotic therapy in maxillofacial fractures reduced the incidence of SSIs in four RCTs.[29–31] This is especially true for open fracture reductions. Single-shot regimens or short protocols (maximum of 24 hours) seemed to have the same, if not better, effect than longer treatments. The studies included fractures related to the dental area of the mandible and not the condylar region. Postoperative continuation of antibiotic therapy was investigated.[32] No reduction in SSI was observed with the addition of postoperative antibiotics to the standard perioperative prophylaxis after surgery for maxillofacial trauma (relative risk [RR], 1.11; 95% confidence interval [CI], 0.86–1.44).[30,33–42]

The subgroup of patients with mandibular fractures (RR, 1.00; 95% CI, 0.62–1.67) or whenever open reduction was needed (RR, 1.21; 95% CI, 0.89–1.63) did not show an increase in SSI if antibiotics were continued beyond the prophylactic dose.[30,34,39,40]

No differences in the reduction of SSI were observed with prolonged antibiotic regimens beyond prophylaxis in a recent systematic review and meta-analysis of 27 studies (<24 hours antibiotic regimen was compared with 24–72 hours and >72 hours) by Habib et al.[43] Overall, 16 studies focused on mandible fractures, four studies on midface fractures, and six studies on orbital fractures.

Another systematic review and meta-analysis by Dawoud et al.[44] compared patients who received AP with those without

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antibiotics. No clear advantages of AP in reducing adverse events were found (RR, 1.38; 95% CI, 0.47–4.03). A prolonged (>1 day) antibiotic regimen and preoperative versus postoperative administration of antibiotics showed no benefit (RR, 0.84 [95% CI, 0.54–1.31] and RR, 1.47 [95% CI, 0.74–2.89], respectively).

Thoracic Trauma

- Antibiotic prophylaxis in healthy patients sustaining blunt thoracic trauma is not indicated (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is not indicated in blunt thoracic trauma patients undergoing chest tube placement (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is indicated in penetrating thoracic trauma patients undergoing chest tube placement (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is indicated in all cases of delayed drainage of retained hemothorax (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is indicated in blunt and penetrating thoracic trauma cases undergoing surgical exploration (thoracotomy/thoracoscopy) (moderate recommendation, intermediate-quality evidence).

Overall, 70% to 90% of patients who suffer from moderate-severe thoracic trauma will need tube thoracostomy.[45] Retained hemothorax and penetrating thoracic trauma are risk factors for the development of pneumonia and empyema.[46,47] The posttraumatic empyema rate is 2% to 25% (*Staphylococcus aureus* is responsible for 35–75% of infections).[9] The rate of infections is not different between prehospital and in-hospital chest tube placement.[48] The role of AP in tube thoracostomy after blunt and penetrating thoracic trauma has been widely investigated. An RCT by Heydari et al.,[49] including 104 patients undergoing tube thoracostomy after blunt trauma, showed no significant impact of AP in preventing empyema and pneumonia. Eleven studies with a total of 1,234 patients showed that AP is effective in reducing overall empyema rates (odds ratio [OR], 0.32; 95% CI, 0.17–0.61) and in penetrating trauma patients (OR, 0.28; 95% CI, 0.14–0.57), although it is less effective in blunt trauma (OR, 1.30; 95% CI, 0.46–3.67). When considering the rates of wound infections and pneumonia, AP is effective in reducing infectious complications (OR, 0.24; 95% CI, 0.12–0.49)[45,47,50–58]

A prospective study analyzed 328 patients with retained hemothorax after blunt trauma. In those who had a chest tube placed, the absence of periprocedural antibiotics associated with Injury Severity Score of >25 and blunt mechanism of trauma were independent predictors of pneumonia (OR, 2.6; 95% CI, 1.3–5.4).[46]

A multicenter prospective observational study analyzing 1,887 patients who underwent chest tube placement after traumatic hemopneumothorax showed no differences in the rate of infectious events between the antibiotic versus the nonantibiotic group (2.2% vs. 1.5% respectively, $p = 0.75$).[59] Antibiotics were not associated with the risk of pneumonia (OR, 1.61; 95%, CI, 0.86–3.03; $p = 0.14$) and empyema (OR, 1.51; 95% CI, 0.42–5.42; $p = 0.53$).[12]

In a low-resource setting, a retrospective study analyzed 1,002 patients with penetrating and blunt trauma regarding the use of AP. There was no statistically significant difference in the incidence of empyema between the two groups.[60]

Abdominal Trauma

- Antibiotic prophylaxis is not indicated in blunt abdominal trauma treated non-operatively (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is indicated in penetrating abdominal trauma, especially in patients undergoing surgical exploration (laparotomy/laparoscopy) (moderate recommendation, intermediate-quality evidence).
- Prolonged AP (24 hours) and/or antibiotic therapy should be considered in patients with hollow viscus injury (moderate recommendation, intermediate-quality evidence).

In abdominal trauma, it is necessary to consider the high risk of contamination and the necessity to clearly define AP and therapy in the case of penetrating trauma and hollow viscus injuries. Before the antibiotic era, the mortality rate of colonic penetrating trauma was 60% to 70%.[61] Several attempts to standardize the indications of AP in abdominal trauma failed[62–64] because of the unclear distinction between AP and antibiotic therapy and the lack of literature on the topic. Many studies underscored the need for anaerobic coverage.[65] In general, no AP should be given to blunt trauma patients unless a hollow viscus injury is suspected. Antibiotic prophylaxis should be given in penetrating trauma, but it should not last more than 24 hours in the absence of hollow viscus injuries; broad-spectrum antibiotics with aerobic and anaerobic bacteria coverage should be preferred, while aminoglycosides should be avoided whenever possible. In the case of hemorrhagic shock and associated acute kidney injury, the dose of antibiotics should be adjusted.[66–95] Hollow viscus injury with contamination should be considered an indication for antibiotic therapy rather than AP. No evidence exists regarding the need for AP in patients with renal injury associated with urine leak without indication of surgery or invasive procedures.[63,65–68]

Important is the golden rule that antibiotic therapy should last for the minimum possible duration that is safe and benefits the patient. In damage-control laparotomy, postoperative antibiotic administration and the presence of hollow viscus injuries were positive predictors of infection (OR, 6.7%; 95% CI, 1.33–33.8 [$p = 0.044$] and OR, 3.45; 95% CI, 1.03–11.5 [$p = 0.02$], respectively), while preoperative administration of antibiotic was a negative predictor of infection (OR, 0.20; 95% CI, 0.05–0.91; $p = 0.037$).[96] Interestingly, neither Injury Severity Score nor damage-control laparotomy were independent predictors of infection. The study, however, did not discriminate between antibiotic therapy and AP, and the heterogeneity of the injuries was significant. A comparative analysis was done between penetrating and blunt trauma patients who underwent trauma laparotomy and followed the prophylaxis guidelines proposed by the Surgical Care Improvement Project or not.[64,97] Results adjusted for confounding factors showed that the group treated according to the Surgical Care Improvement Project guidelines had a lower risk of SSI (OR, 0.43; 95% CI, 0.2–0.94; $p = 0.035$). However, it is unclear which patients received prophylaxis alone and which received antibiotic therapy. The average duration of in-hospital antibiotic therapy (4 vs. 9 days, $p < 0.001$) was considered one of the differences between the

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two groups. This shows the confusion related to the definition of AP and its indications in the trauma literature.

The relationship between the duration of antibiotic therapy for more than 24 hours in penetrating trauma patients in preventing SSI (RR, 1.00; 95% CI, 0.81–1.23), reducing mortality (OR, 1.67; 95% CI, 0.73–3.82), or intra-abdominal infection (RR, 1.23; 95% CI, 0.84–1.80) could not be demonstrated.[24]

Open Fractures

- Antibiotic prophylaxis effectively reduces wound infections in open fractures, and it should be administered as soon as possible (moderate recommendation, intermediate-quality evidence).
- Long-term antibiotic treatment (7–10 days) is ineffective in reducing open fracture wound infection rate (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis longer than 24 hours is not indicated in gunshot-related fractures (moderate recommendation, intermediate-quality evidence).

Long bone open fractures may be the source of acute and chronic infections. Few recommendations about their management exist in international guidelines.[20] Heterogeneity in indications, management, and diagnostic criteria are common issues in the published studies.[23,98–104] Reports showed that several drugs were tested and administered, including penicillin, its derivatives cephalosporines (dicloxacillin, benzylpenicillin, and cloxacillin), and aminoglycosides. No clear definition of prophylaxis exists, and the ideal timing to start AP has also not been clearly determined. Antibiotic administration ranged from 48 hours to 10 days. No investigation of the prophylaxis effects on drug-induced bacterial resistance was performed. Wound infection rates were reported between 13.3% and 22.6% in those receiving AP, which were significantly lower than in those not receiving AP.[23,98–104] However, in some studies, infections occurring within 6 weeks after a surgical intervention were considered early infections. Antibiotic prophylaxis is effective in reducing wound infections (not specifically osteomyelitis), and no benefit seems associated with the duration of prophylaxis for more than 24 hours in gunshot-related fractures. Long-course (7–10 days) antibiotic therapy is not effective in preventing wound infections (not specifically osteomyelitis). Figure 1 shows the decisional algorithm for the use of AP prescription in open fractures.

Burns

- Routine AP in burns patients is not indicated (moderate recommendation, intermediate-quality evidence).
- Routine source control with extensive irrigation for the removal of contaminated material is part of infection prevention in burn patients (moderate recommendation, intermediate-quality evidence).
- No differences exist between systemic and topical AP in preventing infections in burn patients (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis in severe burn patients is indicated in those undergoing endotracheal intubation and mechanical ventilation; it should be ideally administered before the intubation and according to the pharmacokinetics of the chosen antibiotic when possible (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis in severe burn patients may be indicated to prevent split-thickness skin graft infection (moderate recommendation, intermediate-quality evidence).
- There is no indication for routine AP following the debridement of devitalized tissues (moderate recommendation, intermediate-quality evidence).

In burn patients, infections are of paramount importance, as it is a frequent cause of death or skin graft loss (51z). Infections in these patients are often due to multiresistant species. Primary adequate source control (extensive irrigation, temporary coverage of the burned area, and removal of contaminated material) is critical in reducing the risk of infection. Systemic AP in burn patients reduced all-cause mortality (OR, 0.54; 95% CI, 0.34–0.87).[105] Moreover, systemic prophylaxis seems to be related to reducing pneumonia rates (OR, 0.55; 95% CI, 0.36–0.84).[105] Concerning wound infection, a positive effect

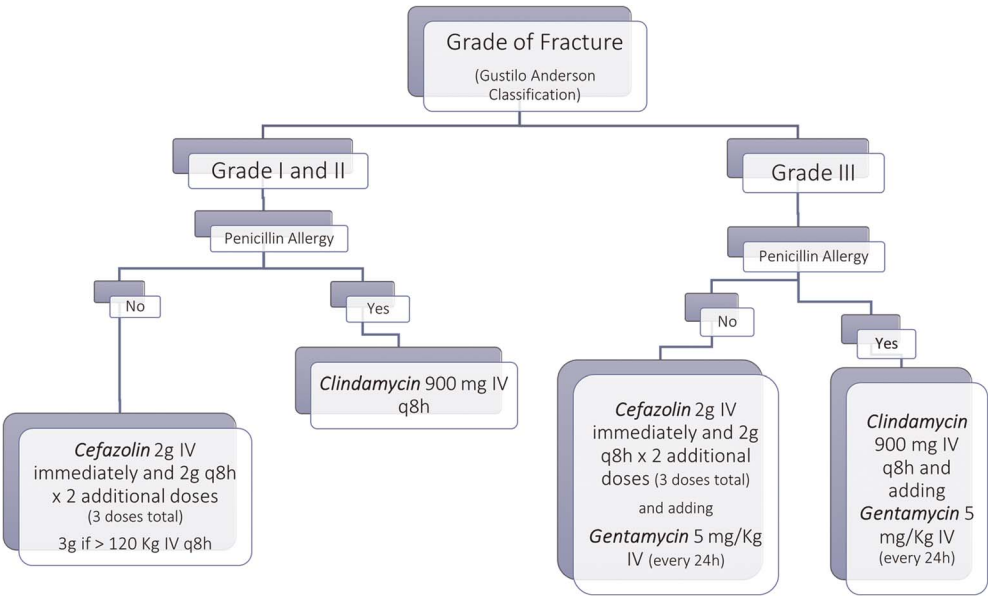
Grade of Fracture
(Gustilo Anderson Classification)
Grade I and II
Grade III
Penicillin Allergy
Penicillin Allergy
No
Yes
No
Yes
Clindamycin 900 mg IV q8h
Cefazolin 2g IV immediately and 2g q8h x 2 additional doses (3 doses total)
3g if > 120 Kg IV q8h
Cefazolin 2g IV immediately and 2g q8h x 2 additional doses (3 doses total)
and adding
Gentamycin 5 mg/Kg IV (every 24h)
Clindamycin 900 mg IV q8h and adding Gentamycin 5 mg/Kg IV (every 24h)

Figure 1. Antibiotic prophylaxis decision algorithm in open fractures.

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of perioperative AP exists (OR, 0.72; 95% CI, 0.52–1.01).[30] Bacteriemia was not affected by any intervention. Antibiotic prophylaxis seems to have a greater effect in reducing gram-positive infections (OR, 0.58; 95% CI, 0.43–0.76) but not those caused by gram-negative species. Great heterogeneity of patients within the different studies exists, making it difficult to consider all these results as definitive. The role of prophylactic topical and systemic antibiotics, nonabsorbable antibiotic regimens, and local prophylactic antibiotics administered via the airway to prevent burn wound infection was investigated by several studies.[106–117] No definitive benefit in systemic or topical AP was found related to sepsis, antibiotic resistance, wound healing, hospital length of stay, or infectious-related mortality. These results apply to both severe (>20% of the body surface area) and less severe (<20% of total body surface area) burn injuries.[118] Topical antibiotic studies evaluated placebo versus neomycin, bacitracin, and polymyxin B. A significant increase in wound infection rate (OR, 1.87; 95% CI, 1.09–3.19) and total length of hospital stay (median, 2.11 days; 95% CI, 1.93–2.28) was observed with silver sulfadiazine. Trimethoprim-sulfamethoxazole alone was associated with a significant decrease in the risk of pneumonia, according to one trial (RR, 0.18; 95% CI, 0.05–0.72), and in general, it seemed beneficial in mechanically ventilated patients as well.[118,119] Nonabsorbable antibiotics seemed to correlate with higher methicillin-resistant *Staphylococcus aureus* rates when associated with cefotaxime (RR, 2.22; 95% CI, 1.21–4.07). No benefits on sepsis or mortality were observed with intratracheally administered antibiotics.

Some benefits in terms of pneumonia-related mortality seemed to be associated with AP in patients with inhalation injury.[120]

Routine use of systemic AP in pediatric burn injury has no beneficial effects.[121] Local or systemic infection rates were similar in the AP and no-antibiotic groups. The same results were observed when the analysis was adjusted for confounding factors (total burn surface area, age, and country income level).[121]

Wound microbiology modifies its components with AP and antibiotic therapy depending on the type of antibiotics used and treatment duration.[122] Multidrug-resistant organisms were found in 39% of patients 1 month from admission. The risk of infection with multidrug-resistant bacteria was very high in patients with <40% of the body surface area burn (OR, 41.7; 95% CI, 2.1–810.7; $p = 0.01$) and in those who received two or more antibiotics (OR, 9.9; 95% CI, 1–92.7; $p = 0.04$).

Skin Wounds and Skin Bites

- Routine AP in skin and soft-tissue injuries is not strictly indicated and should be considered case by case (moderate recommendation, intermediate-quality evidence).
- Routine AP in mammalian bites is not strictly indicated and should be considered case by case (moderate recommendation, intermediate-quality evidence).
- Accurate prevention of viral infectious disease in animal bites must be performed (i.e., rabies virus) (moderate recommendation, intermediate-quality evidence).
- Attention to tetanus immunization must be given (moderate recommendation, intermediate-quality evidence).
- Accurate source control should be accomplished by cleaning, irrigating, and disinfecting wounds in all skin and soft tissue injuries, including all mammalian bites (moderate recommendation, intermediate-quality evidence).

Almost 12 million skin wounds are treated annually in the United States, adding to the count another 1.5 million animal bites.[123] Not administering AP in noncomplicated skin wounds is a well-established practice.[124] Much of the data come from military settings and must be cautiously applied to the civilian environment.[125] Soft tissue injuries are frequently treated in emergency departments. The need for AP, often suggested and used by physicians, needs to be assessed. Broad spectrum AP in open skin and soft tissue combat-related injuries is necessary and beneficial to decrease infection rates and length of hospital stay.[126,127] Data on skin and soft tissue injuries reported a synergistic effect of extensive wound irrigation and AP in decreasing the incidence of infection in moderately and severely contaminated skin and soft tissue injuries.[128] The reported different rates of infections in different management strategies include 17% in irrigation/no AP, 40% in AP/no irrigation, and 75% in no AP/no irrigation group ($p < 0.0005$).

In mammalian bites, clinical results regarding AP are conflicting. It seems that overall AP usage has no significant benefit in mammalian bites. Antibiotic prophylaxis effectively reduces infectious complications in human bites (OR, 0.02; 95% CI, 0–0.33), but no definitive benefits were demonstrated in dog and cat bites. Hand injuries showed a higher complication rate if not treated with AP (2% rate in antibiotic group versus 28% in control (OR, 0.1; 95% CI, 0.01–0.86).[129,130]

CONCLUSION

Antibiotic prophylaxis must be used only when it is indicated. Its overuse has no beneficial effects on patients but has a potential drawback in increasing bacterial resistance. Tailored infection risk calculation for each patient must be performed, with correct source control playing a major role in infection prevention.

AUTHORSHIP

F.C. contributed in the manuscript conception and draft. All authors critically revised the manuscript and contributed with important scientific knowledge, giving the final approval.

DISCLOSURE

Conflicts of Interest: Author Disclosure forms have been supplied and are provided as Supplemental Digital Content (http://links.lww.com/TA/D469).

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